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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/594,453

09/26/2006

Michael Kretschmar

LNK-019

1342

31496

7590

09/02/2009

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EXAMINER

TSAY, MARSHA M

ART UNIT

PAPER NUMBER

1656

NOTIFICATION DATE

DELIVERY MODE

09/02/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chalin@smithpatent.com

Office Action Summary	Application No. 10/594,453	Applicant(s) KRETSCHMAR ET AL.	
	Examiner Marsha M. Tsay	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,4-15,17 and 24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,4-15,17 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 9, 2009, has been entered.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 1, 3, 16, 18-23 are canceled. Claims 2, 4-15, 17, 24 are currently under examination.

Priority: The request for priority to GERMANY 102004044429.3, filed September 14, 2004, is acknowledged.

Objections and Rejections

Claim 8 is objected to because of the following informalities: in claim 8, line 3, the term "is" should be deleted. Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 2, 4-15, 17, 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2(i) recites the limitation "the plasma fraction" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Claims 4-15, 17, 24 are included in this rejection because they are dependent on claim 2 and fail to cure its defect.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2, 4-6, 8, 14, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764; previously cited). For examination purposes, even though claim 2 uses closed claim language "consisting of", the steps of 2(ii) and 2(iii) have been given their broadest and most reasonable interpretation, i.e. one *or more* steps can be encompassed by "removing" and "treating", since steps 2(ii) and 2(iii) do not require a *specific* sub-step or sub-steps for "removing" the fibronectin precipitate in step 2(ii) or for "treating" the composition in step 2(iii). That the "adjusting", "removing", and "treating" steps of claim 2 encompass one *or more sub-steps* is supported by claim 6, which recites the open-ended term "comprises" in the phrase, "wherein removing step (ii) *comprises* stirring the plasma fraction" (emphasis added). Wallace et al. disclose a method for preparing fibronectin and antihemophilic factor from

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blood plasma comprising the steps of: forming a solution of blood plasma fraction in an aqueous medium, acidifying the solution to a pH sufficient to form an acid precipitate, separating the acid-precipitate from the solution, isolating fibronectin from the precipitate, and isolating antihemophilic factor from the solution at a temperature of 2°-20° C (col. 9-10 lines 1-21; claims 2, 4-5, 24). Wallace et al. further disclose that the solution can be acidified at a pH of about 5.0 to form the acid precipitate (col. 9 line 13; claims 2, 4-5). Wallace et al. also disclose the plasma fraction is dissolved cryoprecipitate (col. 9 line 9, col. 5 line 28; claim 14). In Example 1, Wallace et al. disclose the acid precipitate contains 260 g protein in 13 liters of a buffer (col. 5 line 34; claim 8). After precipitation, the precipitate suspension was stirred for 3 hours (col. 5 lines 50-53; claim 6). In col. 4, lines 40-42, Wallace et al. disclose that the precipitate contains a major proportion of the fibronectin (i.e. greater than 50%, preferably greater than 60%). Wallace et al. do not expressly disclose that by practicing the disclosed method, a precipitate is formed and removed, where the precipitate comprises 70-90% of the initial amount of fibronectin.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to separate fibronectin and/or a coagulation factor from a plasma fraction by the method of Wallace et al. as noted above and such that the major proportion of the fibronectin precipitate is composed of fibronectin, (i.e. greater than 60%, 70%, etc.) (claims 2, 4-6, 8, 14, 24). Since Wallace et al. disclose that the percentage of fibronectin in said precipitate is preferably greater than 60%, it would be reasonable for one of ordinary skill to accept that said fibronectin precipitate of Wallace et al. can contain up to 70%, 80%, and even 90% of fibronectin since the range of greater than 60% is disclosed.

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In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990) (The prior art taught carbon monoxide concentrations of "about 1-5%" while the claim was limited to "more than 5%." The court held that "about 1-5%" allowed for concentrations slightly above 5% thus the ranges overlapped.)". Similarly, a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

In their remarks, Applicants assert (1) the closed language of claim 2 precludes the application of the Wallace et al. reference, which describes a complex, multi-step process that includes several distinct steps in addition to those recited in claim 2 as amended herewith, including multiple centrifugation steps to obtain a purified fibronectin substitute precipitate and further cooling steps to precipitate remaining fibronectin, though capturing at most 60% of the fibronectin present in the original plasma fraction. In contrast, the pending claims relate to a simple, one-step titration process that results in the direct quantitative separation of fibronectin from a plasma solution to yield a purified coagulation factor, more particularly a von Willebrand factor (vWF), as well as the high yield recovery of 70 to 99%, more preferably at least 90% of the fibronectin present in the plasma fraction. (2) In addition, the Wallace et al. method requires the preparation of fibronectin and fibronectin substitutes from an "acid-chill precipitate", at temperature ranging from 2.5 to 7.5° C. In contrast, the steps of the inventive process are

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performed at room temperature, i.e. at temperatures ranging from 20° C to 25° C, which allegedly achieve unexpected superior results that could not have been predicted by one of ordinary skill in the art. Applicant's arguments have been fully considered but they are not persuasive.

(1) Reply: As explained in the beginning of the instant 103(a) rejection, even though claim 2 uses closed claim language “consisting of”, the steps of 2(ii) and 2(iii) have been given its broadest and most reasonable interpretation, i.e. multiple steps can be encompassed by “removing” and “treating”, since steps 2(ii) and 2(iii) do not recite how the fibronectin precipitate is “removed” in step 2(ii) and how the composition is “treated” in step 2(iii).

Wallace et al. disclose the fibronectin precipitate contains a major proportion of fibronectin, i.e. greater than 50%, preferably greater than 60% (col. 4 lines 40-42). As noted in the 103(a) rejection above, it would be reasonable for one of ordinary skill to expect that a fibronectin precipitate having greater than 50% or 60% fibronectin would encompass the values of 70%, 80%, 90% fibronectin and there is no evidence of record to the contrary.

(2) Reply: Wallace et al. *expressly* disclose that the acid-chill precipitate can be at a temperature of about 2°-20° C (col. 9 line 14), which overlaps with the instantly recited range of 20° C to 25° C. As such, by practicing the method of Wallace et al. at 20°, which is expressly taught by the reference, the desired percentage of fibronectin in the precipitate would have been achieved. Moreover, because Wallace et al. acknowledges that greater than 60% fibronectin can be achieved by practicing the method at a temperature including 20°, the resulting percentage of fibronectin removed would not be unexpected.

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For at least these reasons, the Wallace et al. reference is still believed to be relevant 103(a) art.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764). The teachings of Wallace et al. are outlined above. Wallace discloses the acid-precipitate was separated by centrifugation. Wallace et al. do not teach separation by means of an agitator blade of a stirrer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recognize that the separation of the acid-precipitate from the plasma fraction can be carried out by any acceptable means known in the art, including the blade of a stirrer, since techniques for separating a precipitate from a solution are routine in the art (claim 7).

Applicant's remarks regarding Wallace et al. has been considered but are not found to be persuasive.

Applicant does not dispute that it would have been well-known at the time of the invention to substitute centrifugation as taught by Wallace with using an agitator blade of a stirrer as a method of removing the precipitate and there is no evidence of record to suggest otherwise. As such, the rejection is maintained for the reasons of record and the reasons set forth above.

Claims 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764; previously cited) in view of Newman et al. (US 5710254). The teachings of

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Wallace et al. are outlined above. It is known in the art that cryoprecipitated plasma fractions are prepared with suitable buffers in order to purify out coagulation factors. Even so, Wallace et al. do not expressly teach initial concentrations of NaCl or glycine.

Newman et al. disclose that a cryoprecipitate can be prepared from normal human plasma where said cryoprecipitate has an initial concentration of 60 mM glycine and 40 mM NaCl prior to treatment to obtain vWF (von Willebrand factor). See column 2, lines 29-31.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the sodium-glycine buffer of Newman et al. into the initial preparation of the cryoprecipitate of Wallace et al. (claims 9-13). The motivation to do so is to obtain an initial plasma fraction preparation that will yield the most stable environment and preserve the activity of the blood factors that one of ordinary skill would like to purify.

Claims 15, 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764; previously cited) in view of Burnouf-Radosevich et al. (US 5408039; previously cited). The teachings of Wallace et al. are outlined above. Wallace et al. do not teach purification steps of the cryoprecipitated plasma fraction or vWF.

Burnouf-Radosevich et al. disclose a process for purifying human von Willebrand factor (vWF) from a cryoprecipitated plasma fraction, which comprises a series of purification steps (col. 5-7). Burnouf-Radosevich et al. disclose aluminum hydroxide treatment to remove fibronectin (col. 5 lines 43-49), a solvent-detergent treatment to destroy lipid enveloped viruses (col. 5 lines 57-60), and an anion exchange chromatographic step (col. 6). After the anion

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exchange chromatographic step, Burnouf-Radosevich et al. disclose that the vWF eluate reveals a slight contamination by fibronectin (col. 6 lines 66-68).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Wallace et al. by substituting the purification steps of Burnouf-Radosevich et al. to a plasma fraction for the separation of fibronectin and a coagulation factor (vWF) (claims 15, 17). The motivation to do so is given by Burnouf-Radosevich et al., which discloses further purification steps of plasma fraction in the separation of fibronectin and a different coagulation factor than that of Wallace et al. (i.e. vWF). It would be reasonable for one of ordinary skill to recognize that additional purification steps of Burnouf-Radosevich et al. would yield a purer protein product and that since Wallace et al. already disclose the separation of a coagulation factor; a specific factor (i.e. vWF) can therefore be separated.

Applicant's remarks regarding the Wallace et al. has been considered but are not found to be persuasive.

The reasons for maintaining the Wallace et al. reference is the same as noted above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

August 27, 2009

/David J. Steadman/
Primary Examiner, Art Unit 1656